

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

| | |
|---|---|
| Date of mailing (day/month/year) 11 July 2001 (11.07.01) | |
| International application No. PCT/US00/22094 | Applicant's or agent's file reference 1381/00055 |
| International filing date (day/month/year) 14 August 2000 (14.08.00) | Priority date (day/month/year) 13 August 1999 (13.08.99) |
| Applicant ANANTHAN, Subramaniam | |

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

13 March 2001 (13.03.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

| | |
|---|----------------------------------|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland | Authorized officer H. Zhou |
| Facsimile No.: (41-22) 740.14.35 | Telephone No.: (41-22) 338.83.38 |

PATENT COOPERATION TREATY

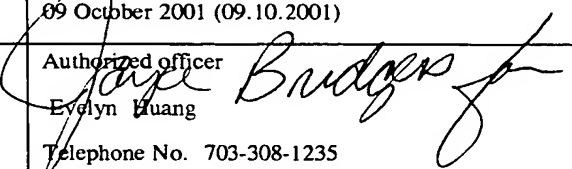
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REC'D 06 NOV 2001

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

PCT

(PCT Article 36 and Rule 70)

| | | | |
|--|---|--|--|
| Applicant's or agent's file reference 1381/00055 | | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) | |
| International application No. PCT/US00/22094 | International filing date (day/month/year) 14 August 2000 (14.08.2000) | Priority date (day/month/year) 13 August 1999 (13.08.1999) | |
| International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 31/485; C07D 489/08, 491/22, 495/18, 495/22; A61P 25/04, 37/02 and US Cl.: 514/279; 546/39, 40 | | | |
| Applicant SOUTHERN RESEARCH INSTITUTE | | | |
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>3</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of ___ sheets.</p> | | | |
| <p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p> | | | |
| Date of submission of the demand 13 March 2001 (13.03.2001) | | Date of completion of this report 09 October 2001 (09.10.2001) | |
| Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230 | | Authorized officer  Evelyn Huang Telephone No. 703-308-1235 | |

Form PCT/IPEA/409 (cover sheet)(July 1998)

I. Basis of the report**1. With regard to the elements of the international application:***

- ☒ the international application as originally filed.
- ☒ the description:
pages 1-26 _____ as originally filed
pages NONE _____, filed with the demand
pages NONE _____, filed with the letter of _____.
- ☒ the claims:
pages 27-29 _____, as originally filed
pages NONE _____, as amended (together with any statement) under Article 19
pages NONE _____, filed with the demand
pages NONE _____, filed with the letter of _____.
- ☐ the drawings:
pages NONE _____, as originally filed
pages NONE _____, filed with the demand
pages NONE _____, filed with the letter of _____.
- ☐ the sequence listing part of the description:
pages NONE _____, as originally filed
pages NONE _____, filed with the demand
pages NONE _____, filed with the letter of _____.

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. STATEMENT**

| | | |
|-------------------------------|--------------------|-----|
| Novelty (N) | Claims <u>1-16</u> | YES |
| | Claims <u>NONE</u> | NO |
| Inventive Step (IS) | Claims <u>NONE</u> | YES |
| | Claims <u>1-16</u> | NO |
| Industrial Applicability (IA) | Claims <u>1-16</u> | YES |
| | Claims <u>NONE</u> | NO |

2. CITATIONS AND EXPLANATIONS

Claims 1-16 lack an inventive step under PCT Article 33(3) as being obvious over WO96/02545 (SMITHKLINE BEECHAM FARMACEUTICI S.P.A.) wherein a morphinoid compound is generically disclosed. The instant compound I is encompassed by the product compound of Scheme 8 (page 7) whereas the instant compound II is embraced by the product compound of Scheme 6 (page 6), wherein R1 is cyclopropylmethyl, R2 and R3 are hydroxy, R4 and R5 together form an oxy, R6 is hydrogen and at least one of X, Y, R in compound I is other than hydrogen. To one of ordinary skill in the art, choosing one among many is prima facie obvious in the absence of unexpected results.

Claims 1-16 meet the criteria set out in PCT Article 33(2), because the prior art does not specifically teaches the instant compound of formula I or II.

Claims 1-16 meet the criteria set out in PCT Article 33(4), because the inventive compound finds industrial applicability as an immuno-modulatory agent, and as an agent in the treatment of pain or drug abuse.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/22094

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : Please See Extra Sheet.

US CL : 514/279; 546/39, 40

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/279; 546/39, 40

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAS ONLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|---|-----------------------|
| X | WO 96/02545 A1 (SMITHKLINE BEECHAM FARMACEUTICI S.P.A.) 01 February 1996, see entire document, especially pages 6-7, Scheme 5, Scheme 6 and Scheme 8. | 1-16 |
| A | US 5,223,507 A (DAPPEN et al.) 29 June 1993, see entire document, especially columns 13-22, Table I. | 1-16 |
| A | US 4,816,586 A (PORTOGHESE) 28 March 1989, columns 1-2. | 1-16 |

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

| | |
|---|--|
| * Special categories of cited documents: | *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention |
| *A* document defining the general state of the art which is not considered to be of particular relevance | *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone |
| *B* earlier document published on or after the international filing date | *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | *A* document member of the same patent family |
| *O* document referring to an oral disclosure, use, exhibition or other means | |
| *P* document published prior to the international filing date but later than the priority date claimed | |

Date of the actual completion of the international search

18 SEPTEMBER 2000

Date of mailing of the international search report

13 OCT 2000

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
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Authorized officer

EVELYN HUANG

Telephone No. (703) 308-1235

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/22094

A. CLASSIFICATION OF SUBJECT MATTER:
IPC (7):

A61K 31/485; C07D 489/08, 491/18, 491/22, 495/18, 495/22; A61P 25/04, 37/02